

### REMARKS

Claims 12-22 and 27-49 are pending. In view of their amendment (i.e., reformatting “use” claims as methods of treatment), the rejoinder of claims 21-22 and 27-28 is requested. Applicants cancel non-elected claims 8-11 and 24-25 without prejudice to future prosecution of that subject matter.

The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Claim 12 is amended by incorporating the limitations of claim 13 and at least the mutation KKK191-193AAA from claim 18. New claim 33 is a combination of original claims 12-15. New claim 40 is a combination of original claims 12-13 and 18. The “prodrug” is defined as zymogen protein C. The “variant” is defined as mutant activated or zymogen protein C comprised of at least one mutation with reduced anticoagulant activity.

Paper and computer readable forms of the Sequence Listing do not add new matter, and their contents are the same. It is respectfully submitted that the attached complies with 37 CFR § 1.821 et seq. Otherwise, prompt notice of any defects in the Sequence Listing is earnestly solicited and additional time is requested to comply.

To satisfy their duties of candor and good faith, Applicants bring to the attention of the Examiner related subject matter in Application Nos. 11/589,371 and 12/391,082. They are not commonly owned. The Examiner is invited to consider their prosecution histories and the prior art of record in those applications, which are accessible through the Image File Wrapper (IFW), in view of the Federal Circuit’s holding in *McKesson Information Solutions v. Bridge Medical*, 82 USPQ2d 1865 (Fed. Cir. 2007). To avoid duplication of those materials in the PTO’s records, reference to the IFW is encouraged but Applicants would be ready to submit copies of these materials for the Examiner’s review if he prefers.

### 35 U.S.C. 112 – Definiteness

Claims 12 and 19-20 were rejected under Section 112, second paragraph, as allegedly “indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Applicants traverse.

The term “providing” is deleted from claim 12 to correct a typographical error.

Claim 19 is amended to clarify that the effective amount of the mutant activated or zymogen human protein C (hPC) does not provide a therapeutic effect in the subject as an anticoagulant, profibrinolytic, or antithrombotic agent. Human protein C with at least one mutation KKK191-193AAA has reduced anticoagulant activity (see page 39, lines 9-28, of the present specification).

The Examiner requested recitation of a reference sequence in claim 20. The reference sequence for zymogen hPC starts at residue 43 of the amino acid sequence in U.S. Patent 4,775,624 (in the nascent polypeptide, the signal peptide is residues 1-33 and the pro peptide is residues 34-42). Support for the amendment is found at page 17, lines 26-32, of the present specification. The locations of the three lysines and two arginines, which may be mutated, are marked in the attached. The skilled person knows the wild-type amino acid sequence of protein C, and its relationship to zymogen hPC and activated hPC (APC) forms.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

### *35 U.S.C. 112 – Written Description*

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). A specification need not teach, and preferably omits, what is well known in the art. See *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81, 94 (Fed. Cir. 1986).

Claims 12-20 and 29-32 were rejected under Section 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse because the specification teaches a representative number of species within the claimed genus. The present amendment specifying activated hPC, zymogen hPC, or

mutant activated or zymogen hPC moots this rejection. In particular, a representative number of mutations are known as shown, for example, in Gale et al. (*J. Biol. Chem.* 277:28836-28840, 2002).

Withdrawal of the written description rejection is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

### 35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 12-14, 16-17, 19 and 29-32 were rejected under Section 102(b) as allegedly anticipated by Griffin et al. (WO 01/56532). Applicants traverse because a limitation of claim 20, which was listed in this rejection, is incorporated into independent claim 12 by requiring the mutation KKK191-193AAA. Since this limitation is also incorporated in all claims depending from claim 12, this rejection is moot.

Claims 12, 14, 16-19 and 29-32 were rejected under Section 102(b) as allegedly anticipated by Ciaccia (WO 01/72328). Applicants traverse because a limitation of claim 20, which was listed in this rejection, is incorporated into independent claim 12 by requiring the mutation KKK191-193AAA. Moreover, claim 18 is reformatted as an independent claim and requires a human source. Since this limitation is also incorporated in all claims depending from claim 12, this rejection is moot.

Claims 12-13, 19, 29 and 32 were rejected under Section 102(b) as allegedly anticipated by Griffin et al. (U.S. Patent 5,084,274). Applicants traverse because a limitation of claim 20, which was not listed in this rejection, is incorporated into independent claim 12 by requiring the mutation KKK191-193AAA. Since this limitation is also incorporated in all claims depending from claim 12, this rejection is moot.

Applicants request withdrawal of the Section 102 rejections because the cited documents fail to disclose all limitations of the claimed invention.

*35 U.S.C. 103 – Nonobviousness*

A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* (“Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue”). Prima facie obviousness also requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 12-17, 19 and 29-32 were rejected under Section 103(a) as allegedly unpatentable over Griffin et al. (WO 01/56532) in view of Kureshi et al. (Neurosurgery 35:822-830). Applicants traverse because a limitation of claim 20, which is impliedly not considered obvious since it was not listed in this rejection, is incorporated into independent claim 12 by requiring the mutation KKK191-193AAA. Since this limitation is also incorporated in all claims depending from claim 12, this rejection is moot.

Applicants request withdrawal of the Section 103 rejection because the claims would not have been obvious to one of ordinary skill in the art.

*Double Patenting*

Claims 12-14, 16, 19, 29-30 and 32 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-7 of Patent No. 7,074,402. The '402 patent is assigned to the University of Southern California and the Scripps Research Institute (TSRI). But this application is assigned to TSRI, the Uni-

versity of Rochester, and Socratech LLC. Since there is no common ownership of the '402 patent and this application, a double patenting rejection is improper.

Claims 12-13, 16-19, 28 and 32 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-36 of Patent No. 5,084,274. The '274 patent is assigned to the Scripps Research Institute (TSRI). But this application is assigned to TSRI, the University of Rochester, and Socratech LLC. Since there is no common ownership of the '274 patent and this application, a double patenting rejection is improper.

Claims 12-17, 19-20 and 29-32 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 8-12 and 60-66 of copending Application No. 10/886,766. The '766 application is assigned to the Scripps Research Institute (TSRI). But this application is assigned to TSRI, the University of Rochester, and Socratech LLC. Since there is no common ownership of these applications, a double patenting rejection is improper.

Claims 12-17, 19-20 and 29-32 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-12 and 42-49 of copending Application No. 11/589,371. The '371 application is assigned to the Scripps Research Institute (TSRI). But this application is assigned to TSRI, the University of Rochester, and Socratech LLC. Since there is no common ownership of these applications, a double patenting rejection is improper.

Claims 12-14, 16-19, 28 and 32 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-16 of copending Application No. 11/632,850. The '850 application is assigned to the University of Rochester. But this application is assigned to the Scripps Research Institute, the University of Rochester, and Socratech LLC. Since there is no common ownership of these applications, a double patenting rejection is improper.

Therefore, Applicants request withdrawal of the double patenting rejections.

*Conclusion*

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_



Gary R. Tanigawa  
Reg. No. 43,180

901 North Glebe Road, 11th Floor  
Arlington, VA 22203-1808  
Telephone: (703) 816-4000  
Facsimile: (703) 816-4100